Applicant: Abelardo Silva et al.

Filed: 08/16/2006

Serial No.: 10/550,715 Page 3 of 10

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application:

- 1-17 (Canceled)
- 18. (Original) An isolated complex of the Formula I or Formula II:

$$[(AV)_m-L1]_{n-}P_r \qquad I$$

$$AV$$
— $[L2-(Pr)_o]_p$ II

wherein:

m is an integer from 1-5;

n is an integer from 1-100;

o is an integer from 1-5;

p is an integer from 1-100;

AV is an antiviral compound;

L1 and L2 are polyvalent linkers covalently linking AV to Pr, or where L1 and L2 are absent;

Pr is a protein; and

wherein the complex possesses antiviral activity in vivo.

- 19. (Original) The complex of Claim 18, wherein the antiviral compound is a peptide.
- 20. (Original) The complex of Claim 19 wherein the peptide has a mass of less than about 100 kDA.
- 21. (Original) The complex of Claim 19, wherein the peptide has a mass of less than about 30 kDA.

Applicant: Abelardo Silva et al. Serial No.: 10/550,715 Filed: 08/16/2006 Page 4 of 10

22. (Original) The complex of Claim 19, wherein the peptide has a mass of less than about 10 kDA.

- 23. (Original) The complex of Claim 19 wherein the peptide is a peptidomimetic.
- 24. (Currently Amended) The complex of Claim 19 wherein the peptide consists of up to 51 amino acids comprising a sequence selected from the group consisting of:

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6, SEQ ID NO: 843;

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7, SEQ ID NO: 844;

Y1-X-X-Y2-X-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8, <u>SEQ ID NO: 844;</u>

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9, <u>SEQ_ID_NO:</u> 846;

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10, <u>SEQ_ID</u> NO: 847;

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11, <u>SEQ ID NO: 848</u>;

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12, SEQ ID NO: 849;

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13, SEQ ID NO: 850;

Y1-X-X-Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14, <u>SEQ ID NO: 851;</u>

Y2-X-X-Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14, <u>SEQ ID NO: 852;</u>

Y3-X-X-Y4-X-X-Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14, SEQ ID NO: 852;

Y4-X-**Y5-**X-**Y6-Y7-**X-**X-**Y**8-**X-**Y9-Y10-**X-**X-Y11-Y12-**X-**X-Y13-Y14,** <u>SEQ ID</u> NO: 854;

Y5-X-X-Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14, <u>SEQ ID NO: 855;</u> Y6-Y7-X-X-Y8-X-Y9-Y10-X-X-Y11-Y12-X-X-Y13-Y14, <u>SEQ ID NO: 856;</u> Applicant: Abelardo Silva et al.

Filed: 08/16/2006

Serial No.: 10/550,715 Page 5 of 10

W-X-X-W-X-X-I-X-X-T-X-X-I-X-X-L-I-X-X-Q-X-Q-Q-X-X-N; W-X1-X2-W-X3-X4-X5-I-X6-X7-X8-T-X9-X10-I-X11-X12-L-I-X13-X14-X15-Q-X16-Q-Q-X17-X18-N-X19-X20-X21-X22-X23, <u>SEQ ID NO: 857</u>;

peptide DP178 (T-20); and

peptide T-1249;

wherein:

X1 is selected from the group consisting of M, L, I, Q, T, R and K;

X2 is either E, D, Q and K;

X3 is selected from the group consisting of E, D and K;

X4 is selected from the group consisting of K, R, E, Q, N and T;

X5 is selected from the group consisting of E, L, R, K and Q;

X6 is selected from the group consisting of N, D, S, E, Q, K, R, H, T, I and G;

X7 is selected from the group consisting of N, Q, D, E, K, S, T and Y;

X8 is selected from the group consisting of Y, F, H, I, V and S;

X9 is selected from the group consisting of G, K, R, H, D, E, S, T, N and Q;

X10 is selected from the group consisting of K, H, E, Q, T, V, I, L, M, A, Y, F, and P;

X11 is selected from the group consisting of H, K, E, Y and F;

X12 is selected from the group consisting of T, S, Q, N, E, D, R, K, H, W, G, A, and M;

X13 is selected from the group consisting of D, E, Q, T, K, R, A, V and G;

X14 is selected from the group consisting of D, E, K, H, Q, N, S, I, L, V, A and G;

X15 is selected from the group consisting of S, A and (P);

X16 is selected from the group consisting of N, K, S, T, D, E, Y, I and V;

X17 is selected from the group consisting of E, D, N, K, G, and V;

X18 is selected from the group consisting of K, R, H, D, E, N, Q, T, M, I, and Y;

X19 is selected from the group consisting of E, V, Q, M, L, J, and G;

X20 is selected from the group consisting of Q, N, E, K, R, H, L, and F;

X21 is selected from the group consisting of E, D, N, S, K, A, and G;

X22 is selected from the group consisting of L, I, and Y; and

X23 is selected from the group consisting of I, L, M, Q, S, and Y.

Applicant: Abelardo Silva et al.

Filed: 08/16/2006

Serial No.: 10/550,715
Page 6 of 10

25. (Original) The complex of Claim 24 wherein the protein is a blood component.

- 26. (Original) The complex of Claim 25, wherein the blood component is selected from the group consisting of red blood cells, immunoglobulins, IgM, IhG, serum albumin, transferrin, P90 and P38, ferritin, a steroid binding protein, thyroxin binding protein, and α -2-macroglobulin.
- 27. (Original) The complex of Claim 25, wherein the blood component is human serum albumin and the linker is a peptide linker.
- 28. (Original) The complex of Claim 25, wherein the blood component is human serum albumin and the linker is a non-peptide linker.
 - 29. (Canceled)
- 30. (Original) The complex of Claim 18, wherein the linler L1 or L2 is a non-labile linker that is stable toward hydrolytic cleavage in vivo.
 - 31-47. (Canceled)
- 48. (Original) An anti-viral composition comprising a non-peptidic anti-viral compound covalently linked to a blood component.
 - 49-52. (Canceled)
- 53. (Original) A method for inhibiting the activity of HIV gp41 and HIV in vivo, the method comprising:

administering to the bloodstream of a mammalian host an isolated conjugate complex of Claim 18, wherein the complex is formed by attaching an antiviral compound to a linker having

Applicant: Abelardo Silva et al.

Serial No.: 10/550,715 Filed: 08/16/2006 Page 7 of 10

at least one reactive functional group which reacts with the protein to form stable covalent bonds; and

wherein the isolated conjugate complex is administered in an amount to maintain an effective therapeutic effect in the bloodstream for an extended period of time as compared to a non-conjugated antiviral compound.

54-80. (Canceled)

81. An isolated complex of the Formula I or Formula II: (Original)

$$[(Ih)_{m}-L1]_{n}-Pr \qquad I$$

$$Ih-[L2-(Pr)_{o}]_{p} \qquad II$$

wherein: m is an integer from 1-5; n is an integer from 1-100; o is an integer from 1-5; p is an integer from 1-100; Ih is a renin inhibitor; L1 and L2 are polyvalent linkers covalently linking Ih to Pr, or where L1 and L2 are absent; Pr is a protein; and wherein the complex possesses renin inhibitory activity in vivo.

82-135. (Canceled)

136. (Original) An isolated compound comprising a pharmacologically active moiety covalently conjugated to a macromolecular carrier,

wherein the carrier is pharmacologically inert,

wherein the linkage between said pharmacologically active moiety and said carrier is stable in vivo,

wherein the intact compound substantially retains the pharmacological activity of said pharmacologically active moiety,

and wherein the active half-life of said compound when administered to a mammal is at least about twice that of said pharmacologically active moiety.

Applicant: Abelardo Silva et al.

Filed: 08/16/2006

Serial No.: 10/550,715
Page 8 of 10

137. (Original) The compound according to claim 136, wherein said macromolecular carrier is a protein.

- 138. (Original) The compound according to claim 136, wherein said macromolecular carrier is an albumin of homologous origin to said mammal.
- 139. (Original) The compound according to claim 138, wherein said albumin is a human serum albumin.
- 140. (Original) The compound according to claim 136, wherein said pharmacologically active moiety is conjugated to said carrier via a linker moiety.
- 141. (Original) The compound according to claim 136, wherein said pharmacologically active moiety is directly linked to said carrier.
- 142. (Original) The compound according to claim 136, wherein at least two pharmacologically active moiety molecules are conjugated to said carrier.
- 143. (Original) The compound according to claim 137, wherein the linkage to said carrier is via a lysine side chain on said carrier.
- 144. (Original) The compound according to claim 137, wherein the linkage to said carrier is via a cysteine side chain on said carrier.
- 145. (Original) The compound according to claim 136, wherein said carrier is HSA and the linkage is via C34 of the HSA.